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EXAMINER	
LEWIS, A	
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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 7/25/96.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire THREE month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 16-21, 31-36, 38, 44-58, 69-134 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☒ Claim(s) 115-119, 127-129, 132 is/are allowed.

☒ Claim(s) 16-21, 31-36, 44, 46-58, 69-73, 75, 76, 79-92, 95-97, 100-114, 120-126, 130, 131, 133, 134 is/are rejected.

☒ Claim(s) 38, 45, 74, 77, 78, 93, 94, 98, 99 is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLLOWING PAGES –

Claims 115-119,127-129,132 are allowed.

Claims 45,74,83-86,104-114,120-126,130,131,133,134 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 45 merely recites an intended result of inhaling a nitric oxide releasing compound in a gas comprising at least 1ppm nitric oxide. Claim 45 does not further limit method claim 44 because there is no recitation of a positive method step which further limits the method defined in claim 44. The following language would be acceptable: --The method of claim 44 further comprising; providing said nitric oxide releasing compound in a gas containing at least 1ppm gaseous nitric oxide for inhalation by a mammal for inhalation.--

Claim 74 should recite --said propellant gas is nitric oxide gas.-- to make clear exactly what gas is being defined.

In claim 83, line 12, "...provided that the setting on said flowmeter is such that the residence half time of NO is said reservoir during use by such a mammal is 15 seconds or less." is merely a statement of intended results and not a positive means plus function limitation which further defines the claimed apparatus. Acceptable language would be as follows: --means including a setting on said flowmeter for ensuring that the residence half time of NO is said reservoir during use by such a mammal is 15 seconds or less--.

In claim 104, line 9, "...provided that the NO2 concentration in said gas mixture at the point of inhalation is less than 12ppm." merely recites an intended result rather than a positive method step. Moreover, "...the point of inhalation..." lacks antecedent basis. Suggested language includes --monitoring the gas mixture prior said providing step for NO2 and measuring its concentration; ceasing to provide said gas mixture to a mammal upon sensing a NO2 concentration in said gas mixture which exceeds 12ppm--.

In claim 110, line 8, "...the concentration of NO2..." lacks antecedent basis. Suggested language includes --prior to providing said oxygen containing gas mixture for inhalation by a mammal, monitoring the oxygen containing gas mixture for NO2 and measuring its concentration--.

In claim 120, line 8, "...provided that the NO2 concentration in said gas mixture at the point of inhalation is less than 12ppm." merely recites an intended result rather than a positive method step. Moreover, "...the point of inhalation..." lacks antecedent basis. Suggested language includes --monitoring the gas mixture prior to inhalation for NO2 and ceasing to provide said gas mixture to a mammal upon sensing a NO2 concentration in said gas mixture which exceeds 12ppm--.

In claim 124, line 8, "...said inhalation..." lacks antecedent basis; moreover, "...said inhalation..." suggests that the act of inhaling and therefore the mammal is being recited as an element in the claimed combination. Suggested language includes --prior to

said step of providing said oxygen containing gas mixture for inhalation by a mammal, monitoring the oxygen containing gas mixture for NO2 and measuring its concentration--.

Claims 45,74, would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112 set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Claim 83 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112 set forth in this Office action.

Claims 38,77,78,93 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16-21,31-36,44,46 are rejected under 35 U.S.C. 103(a)

as being unpatentable over Thompson et al.('305).

As to claim 16, Thompson et al. disclose a method for treating cardiovascular disorders (see abstract), which method comprises identifying a mammal in need of such treatment or prevention, and providing a therapeutically-effective amount of nitric oxide-releasing compound (col.6, line 60-col.7, line 4) to a mammal for inhalation. Inasmuch as Thompson et al. discloses the treatment of cardiovascular disorders including pulmonary hypertension (col.5, lines 30,31), the recited malady, (i.e. pulmonary vasoconstriction which causes pulmonary hypertension) is included as a disorder which may be treated using the disclosed method of providing a therapeutically-effective amount of nitric oxide- releasing compound (col.6, line 60-col.7, line 4) to a mammal for inhalation.

As to claims 17,33,46, Thompson et al. disclose a compound SNAP (col.1, lines 8,37,41,48,51) as the nitric oxide-releasing compound.

As to claims 18,34, Thompson et al. disclose a method of providing a therapeutically-effective amount of nitric oxide-releasing compound (col.6, line 60-col.7, line 4) to a mammal for inhalation as an aerosol.

As to claims 19,20,35,36, the sizes of the aerosol droplets (powder or liquid) in Thompson et al. (col.6, line 60-col.7, line 4) can be arrived at through mere routine obvious experimentation and observation with no criticality seen in the particular droplet sizes being claimed. Thompson et al. additionally disclose a

suitable biologically-compatible carrier (e.g.lactose or starch) at col.7, line 3.

Claim 31 is included in Thompson et al. for the reasons set forth above with respect to claim 16 inasmuch as Thompson et al. also disclose the delivery of a therapeutically-effective amount of nitric oxide-releasing compound (col.6, line 60-col.7, line 4) to a human (col.5, lines 39,40) for inhalation.

As to claim 32, Thompson et al. disclose that the therapeutically-effective amount of nitric oxide-releasing compound is a vasodilator and that the compound be administered via a patient's lungs to relieve pulmonary hypertension which is caused by pulmonary vasoconstriction. It would have been obvious to employ the method of Thompson et al. to treat a plurality of cardiovascular disorders involving vasoconstriction including bronchial asthma.

Claim 44 is included in Thompson et al. for the reasons set forth above with respect to claim 16. The vasodilation of lung vessels using the method of medicament administration disclosed by Thompson et al. would result in improved gas exchange in a patient suffering from pulmonary hypertension due to vasoconstriction of lung vessel.

Claims 47-56,58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weinstein ('419) in view of Higenbottam et al. (Am. Rev. Resp. Dis. Suppl. 137:107, 1988).

Weinstein discloses a method of delivering a pharmacoactive compound into the lungs of a mammal (col.1, lines 29-53), said method comprising providing said compound in the form of a liquid or solid suspended in a gas to a mammal for inhalation.

The difference between Weinstein and claim 47 is the suspension of the pharmacoactive drug in a gas comprising a therapeuticallly amount of nitric oxide.

Higgenbottam et al. teach the delivery of nitric oxide along with air or oxygen to the lungs of mammals for the purpose of vasodilating lungs vessels and reducing pulmonary hypertension.

It would have been obvious to modify Weinstein to employ any well known combination of drugs (which are known to be delivered via the intrapulmonary route) suited to the medical needs of a patient because the use of a combination of drugs is sometimes necessary for a complete treatment of patients as disclosed by Weinsten.

As to claims 48 and 49, the medicament within the canisters of Weinstein is liquid medicament; however, it is well known in the respiratory arts to dispense either liquid or powdered medicament from pressurized medicament containers such as the ones employed in Weinstein.

As to claims 50-53, the particular combination of drugs employed in Weinstein can be arrived at through mere routine obvious experimentation and observation in dependence upon the needs of the particular patient and in dependence upon the

particular ailment being treated.

As to claim 54, Weinstein as modified by Higgenbottam et al. as discussed above additionally discloses a vessel (fig.1 of Weinstein) containing pressurized gas comprising at least 1ppm nitric oxide; a housing (10) defining a lumen (15,13), said vessel being attached to said housing to deliver said gas into said lumen; and a mechanism (canister valves not illustrated) for controllably releasing said gas from said vessel into said lumen; said lumen being configured to route said released gas into the respiratory system of a person, and said device appears to weigh less than approximately 5 kg.

As to claim 55, while Weinstein does not disclose the actual weight of the device illustrated in fig.1, it is submitted that the weight of the device can be arrived at through mere routine obvious experimentation and observation with no criticality seen in the particular weight being claimed.

As to claim 56, since Weinstein discloses that the particular medicament within the canisters is dependent upon the particular illness being treated, it is submitted that the use of any well known gaseous component including gaseous nitrogen may be employed as a catalyst, preservative or propellant.

As to claim 58, the canisters of Weinsten contain pressurized medicament. Inasmuch as such pressurized medicament canisters in the art employ liquid or gaseous propellants, it would have been obvious to employ either a liquid or gaseous propellant as an

obvious matter of design choice with no new or unobvious results accruing.

Claim 57 is rejected under 35 U.S.C. 103(a) as being unpatentable over Weinstein et al. in view of Higgenbottam et al. as applied to claims 47-56,58 above, and further in view of Sackner et al.('577).

The difference between Weinstein et al. as modified by Higgenbottam et al. and claim 57 is a rebreathing chamber.

Sackner et al., in an inhaler device, teach a rebreathing chamber (11 of fig.1) which provides means for storing dispensed medicament in order for a patient to reinhale over several breaths to aid in depositing the aerosolized medicament which has not settled in previous breaths (col.12, lines 61-65).

It would have been obvious to further modify Weinstein et al. to employ any well known means for temporarily storing aerosolized medicament between consecutive inhalations because it would have provided means for storing dispensed medicament in order for a patient to reinhale over several breaths to aid in depositing the aerosolized medicament which has not settled in previous breaths as taught by Sackner et al.(col.12, lines 61-65).

Claims 69-73,75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thompson et al.('305) as applied to claims 16-21,31-36,44,46 above, and further in view of Weinstein et al..

As to claim 69, Thompson et al., as discussed above, also disclose a device comprising a vessel containing a nitric oxide-donor compound including a propellant (col.6, line 60-col.7, line 4) and a mechanism for controllably releasing said propellant and nitric oxide-releasing compound.

The difference between Thompson et al. and claim 69 is a housing defining a port into which said vessel is mounted and a lumen in communication with said port.

Weinstein et al. teach a housing (10) defining a lumen (15,13), said vessel being attached to said housing to deliver said gas into said lumen.

It would have been obvious to employ any well known device for the delivery of the drug in Thompson et al. including the use of the device of Weinstein et al..

As to claim 70, the medicament within the canisters of Weinstein is liquid medicament; however, it is well known in the respiratory arts to dispense either liquid or powdered medicament from pressurized medicament containers such as the ones employed in Weinstein.

As to claim 71, Thompson et al. disclose the nitric oxide-donor compound as being suspended in a propellant or dissolved in a carrier (col.6, line 60-col.7, line 12).

As to claim 72, Thompson et al. as discussed above teach the use of SNAP as the nitric oxide-donor compound.

Claims 73 and 75 are included in Thompson et al. as modified

by Weinstein et al. for the reasons set forth above with respect to claims 69,72.

Claims 76,79-82,92,95-97,100-103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walstrom et al.('138) in view of Higgenbottam et al..

The difference between Walstrom et al. and claim 76 is nitric oxide gas.

Higgenbottam et al. teach the delivery of nitric oxide along with air or oxygen to the lungs of mammals for the purpose of vasodilating lungs vessels and reducing pulmonary hypertension.

It would have been obvious to modify Walstrom et al. to employ any well known combination of drugs (which are known to be delivered via the intrapulmonary route) suited to the medical needs of a patient because the use of a combination of drugs is sometimes necessary for a complete treatment of patients as disclosed by Walstrom et al.(figs.2,4).

As to claims 79-82, the particular constituency of a given source of pressurized medicament gas in Walstrom et al. as modified by Higgenbottam et al. can be arrived at through mere routine obvious experimentation and observation. It is well known in the medical arts to combine a plurality of chemicals with a given active ingredient in order act as a preservative, catalyst or to create an optimal environment in which the active ingredient may function optimally for example. With respect to claim 82, Walstrom

et al. illustrate a tracheal tube (32) to deliver the medicaments to a patient; however, it is submitted that it would have been obvious to employ any well known means for delivering medicaments to a patient including the use of a respiratory mask.

As to claim 92, Walstrom et al. as modified by Higgenbottam et al. teach an apparatus for introducing NO gas into the respiratory system of a patient, comprising a source of NO gas (#16 of Walstrom et al.), a ventilator comprising a ventilation circuit (figs.1,2 of Walstrom et al.); and means (20 of Walstrom et al.) for controllably releasing said gas into said ventilation circuit.

As to claims 95,96, the particular constituency of a given source of pressurized medicament gas in Walstrom et al. as modified by Higgenbottam et al. can be arrived at through mere routine obvious experimentation and observation. It is well known in the medical arts to combine a plurality of chemicals with a given active ingredient in order act as a preservative, catalyst or to create an optimal environment in which the active ingredient may function optimally for example.

Claim 97 is included in Walstrom et al. as modified by Higgenbottam et al. for the reasons set forth above with respect to claims 76,92. Walstrom et al. additionally teach a housing (20) equipped with a flowmeter (col.5, line 10+).

As to claims 100-103, the particular constituency of a given source of pressurized medicament gas in Walstrom et al. as modified by Higgenbottam et al. can be arrived at through mere routine

obvious experimentation and observation. It is well known in the medical arts to combine a plurality of chemicals with a given active ingredient in order act as a preservative, catalyst or to create an optimal environment in which the active ingredient may function optimally for example. With respect to claim 103, Walstrom et al. illustrate a tracheal tube (32) to deliver the medicaments to a patient; however, it is submitted that it would have been obvious to employ any well known means for delivering medicaments to a patient including the use of a respiratory mask as an obvious matter of design choice with no new or unobvious results accruing.

Claims 87-91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walstrom et al. in view of Higgenbottam et al. as applied to claims 76,79-82,92,95-97,100-103 above, and further in view of Gauthier et al.('991).

The difference between Walstrom et al. as modified by Higgenbottam et al. and claim 87 is an enclosure suitable for providing an ambient atmosphere from which a patient can inhale.

Gauthier et al., in an apparatus for introducing an aerosol into the respiratory system of a patient, teach an enclosure (12,13) for providing an ambient atmosphere from which a patient can inhale.

It would have been obvious to further modify Walstrom et al. to deliver aerosol to patients using any well known means in the respiratory arts including an enclosure as taught by Gauthier et

al. as an obvious matter of design choice with no new or unobvious results accruing.

As to claims 88-91, the particular constituency of a given source of pressurized medicament gas in Walstrom et al. as modified by Higgenbottam et al. can be arrived at through mere routine obvious experimentation and observation. It is well known in the medical arts to combine a plurality of chemicals with a given active ingredient in order act as a preservative, catalyst or to create an optimal environment in which the active ingredient may function optimally for example. With respect to claims 90,91, Walstrom et al. illustrate a tracheal tube (32) to deliver the medicaments to a patient; however, it is submitted that it would have been obvious to employ any well known means for delivering medicaments to a patient including the use of a respiratory mask or a tent.

Applicant's arguments with respect to claims 16-21,31-36,38,44-58,69-134 have been considered but are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication should be directed to Aaron J. Lewis at telephone number (703) 308-0716.

Aaron J. Lewis
November 12, 1996

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